A CLINICAL GUIDE TO PROGNOSIS IN STRESS DISEASES

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A guide to prognosis in stress diseases has been devised on the basis of experience in the treatment of 739 patients in the Medicine A clinic of the New York Hospital. Its validity has been tested in three selected groups of patients with essential hypertension, migraine, and asthma. An earlier report of the experience of this clinic [1] emphasized a description of the general methods of treatment used, an appraisal of the effectiveness of each, and an estimation of the important prognostic factors. In the present report a more systematic appraisal of prognosis is offered in the form of a score sheet on which a patient can be rated after the first three or four visits to the physician.

Most of the patients were seen at approximately weekly intervals during the first month of attendance at the clinic and at biweekly or monthly intervals thereafter. The average number of visits per patient was 15; the average duration of treatment was nine months. Among these patients 90 had essential hypertension, 62 irritable colon, 67 bronchial asthma, 54 headache due to sustained muscle contraction, 52 migraine, 35 peptic ulcer syndrome, 25 urticaria, 21 vasomotor rhinitis, and 18 ulcerative colitis.

The first step in construction of the scale was to summarize the data in each case under 49 main headings as follows:

Age	Estimate of previous life experience
Admission information (sex, marital status, and employment)	Stress situation in past
Race, nationality	Previous treatment
Religion	Life situation precipitating present illness
Doctors in charge	Estimate of information
System review	Duration of illness
Past medical history	Intensity of illness
Diagnostic headings	Patient's attitude toward illness on admission
Family (general information)	Patient's attitude toward illness during treatment
Spouse	Patient's attitude toward treatment on admission
Children	Patient's attitude toward treatment during course of treatment
Whether contraception used and what type	Course
Childhood	Mood during course
School attendance	Therapy by physician
School adjustment	Therapy by social workers
Mother	Reasons for leaving clinic
Father	Result on leaving clinic
Family values	Appraisal of those still in clinic
Siblings	Follow-up first year
Employment	Follow-up second year
Employment adjustment	Number of visits
Sex, childhood	Number of months
Sex, adult	Clinic financial rating
Housing	
Character attitude	
Character behavior	

These 49 headings were subdivided into 852 items that pertained to the life experience and personal attributes of the patients. The selection of these items was based on the general experience of the entire group of 18 clinic physicians and on their particular experience with the patients of Medicine A clinic over the period of three years. The appropriate item under each heading was checked by the physician in a manner suitable for analysis with an IBM machine.

Independent of the construction of the prognostic scale, an appraisal of the clinical status of each of the 739 patients was made by his physician at yearly intervals or on the patient's discharge or departure from the clinic. The rating was based on changes in signs and symptoms and changes in the way in which the patient saw himself in relation to his life problems and how he handled and reacted to them. Evidence of change in such basic attitudes was adduced from observation of the patient's responses to new situations of significance similar to those that had earlier been associated with symptoms.

On the basis of these clinical appraisals the patients were classified into three groups: 1. Unimproved; these patients displayed no change in either symptoms or attitudes. 2. Moderately or symptomatically improved; these patients displayed a lessening or absence of symptoms without change in basic attitudes. 3. Basically improved; these patients not only were symptomatically improved but displayed a change for the better in their way of dealing with problem situations. The 739 patients fell into the three groups as follows: unimproved, 249, or 34%; symptomatic improvement, 311, or 42%; and basic improvement, 179, or 24%.

These clinical progress appraisals were entered on IBM cards together with the data on life experience and personal attributes as noted above. The various categories, unimproved, symptomatically improved, and basically improved, were then analyzed by the IBM sorting machine so that we might determine which of the coded items were most prevalent in each. Whenever there was a correlation between one of these items and the percentage of patients that fell into the improved groups, the item was selected as possibly significant. The number of items was reduced until those that appeared to be the most significant remained. The prognostic scale was made up of these remaining items, which were weighted in a more or less arbitrary way. It was not possible to evaluate statistically the significance of the various correlations, in view of the extreme variability in numbers and often the very small numerical differences. In addition to the items selected from the code, certain others of presumed significance were arbitrarily added and suitably weighted on the basis of the general clinical impression of the physicians involved.

Groupings were made under three main headings: (1) objective data relating to such items as the patient's age, social status and past medical history (20 points); (2) factors concerning the patient's family and interpersonal

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The following physicians gave us the benefit of their clinical judgment with respect to their own patients: Drs. Jacob Bornstein, George Draper, Charles Duncan, William J. Grace, David T. Graham, Andrew D. Hart Jr., Lawrence E. Hinkle Jr., Thomas Holmes, Robert Marcussen, Herbert S. Ripley, Edward Shepard, Harry Stalker, Ian Stevenson, Leonard Straub, Arthur Sutherland, and Theodore Treuting.

1. Ripley, H. S.; Wolf, S., and Wolff, H. G.: Treatment in a Psychosomatic Clinic: Preliminary Report, J. A. M. A. **138**:949 (Nov. 27) 1948.

relationships obtained from verbatim statements made by the patient (30 points); and (3) evaluations of the patient's past performance, personality structure, and attitude toward his illness, made by the physician (40 points). Table 1 shows the prognosis scale form, with an example of how one patient was scored.

Certain items commonly considered of prognostic importance did not show a positive relationship with clinical appraisals. These items included the sex of the patient, position of the child in the family, bottle or breast feeding, nail biting, night terrors and enuresis in childhood, and the number of visits to the clinic or the frequency or interval between visits. The following factors were used in making up the prognostic scale.

TABLE 1.—*Prognostic Scoring of a Patient in the Group Studied*

Objective Data	Maximum Score	Actual Score	Comment
Age, up to 40 yr	2	2	Age 34
Not divorced or separated	2	2	Married
Third generation American, white, gentile	2	2	American family both sides several generations; gentile
High school education complete	2	2	
Both parents living at home until patient was 12 yr. old	4	4	Father died when patient was 18; mother still alive
No surgical treatment for symptoms	2	0	Caldwell-Lue operation in past
No previous formal psychiatric care	2	2	
Steady employment	2	2	Employed 15 yr. same company
Duration of present illness less than 5 yr.	2	0	Onset of asthma 14 yr. previously
Total	20	16	
Previous health good	1	1	Well until onset of asthma
Some religious education	1	1	Family members of parish (religion no source of conflict)
Emotional support from both parents	4	2	Father and mother "fine people"; mother hypercritical, lives with patient
Congenial siblings	2	1	Brother "more successful"; many tastes in common
Emotional support from spouse	2	2	Wife most understanding and helpful
Sexual compatibility with spouse	2	2	
No serious sexual problem	3	2	One extramarital affair with conflict
Spouse adequate economic provider *	2	..	Not applicable
Children not rejected	2	2	Adopted child after death of own son
No housing problem	2	2	Five-room apartment
Occupational satisfaction	2	2	Proud of his work
Congenial working conditions	2	1	Difficulties with boss and fellow workers
Moderately adequate salary	2	2	Able to meet rent and food costs and furnish home
Goal	3	3	Hope of regaining health and buying home
Total (females) (males)	30 28	23	

Objective Data	Maximum Score	Actual Score	Comment
Evidence from past performance: Not exaggerated sensitivity to traumatic situation; Good interpersonal relationships (including sexual); Evidence that the activities, achievements, and other life experiences have afforded satisfaction	10	5	Adoption of child after death of first; Immature handling of sexual problem, mother, and fellow workers; Job satisfaction
Evidence from personality structure: Moderate flexibility; Minimal and short-lived hostility; Capacity to face and solve personal problems; Active participation in the give and take of daily affairs; Moderate orderliness and reliability; Good judgment and evidence of adequate discrimination regarding human values and goals	10	5	Stubborn; Nurtures small hurts; Inability to face or resolve dependency; hostility conflict; Reliable in meeting financial responsibilities; Reasonable life ambition
Prevailing attitudes of the patient toward illness and his problems at time of admission to clinic: Recognition of failure of present patterns of adjustment and willingness to adopt others; Willingness to consider possibility that life stress, attitudes, and feeling states are relevant to the illness; Confidence in physician, hospital, and its methods; Capacity and willingness to assume responsibility in treatment	10	6	Desperate; Willing to try anything; This hospital last resort; Capacity to assume responsibility for treatment doubtful
Extent to which a specific aspect of the life situation was a factor in precipitating the patient's illness: Extent to which this specific feature is modifiable with regard to the involved person, other persons, and circumstances	10	5	No specific life situation apparently related to onset of illness; wife, child, and job considered assets; mother considered a liability
Total	40	21	

* Scored only for female patients.

OBJECTIVE DATA

The following objective data were rated two points each, except where otherwise indicated.

Age, up to Forty Years.—Patients in their forties and fifties (185) were the ones who showed the least evidence of improvement. The greatest degree of change was found among those from 14 to 40 years of age (537). Those in their sixties (12) and seventies (6) were too few to permit evaluation of them as a group, although great improvement was observed in some.

Not Divorced or Separated.—Only 5% of the 739 patients were either divorced or separated. However, in these two groups (divorced and separated) the percentage of no improvement was 47 and 40, respectively.

Third Generation American, White, Gentile.—The obviously increased adjustment problems of subjects who are not of the dominant group in our society prompted the assignment of two points to third generation American, white, gentile, although the preponderance of patients meeting these criteria among the improved group was slight.

High School Education Completed.—There was a slight preponderance of those with completed high school education among the improved group.

Both Parents Living at Home Until Patient Was Twelve Years Old (Four Points).—Twenty per cent of the patients had suffered the loss of one parent at an early age. In these patients the degree of improvement was much less than for the group as a whole.

No Surgical Treatment for Symptoms.—There were 120 patients among the 739 who had never had any surgery; the incidence of improvement among these was much higher than among the 117 who had had one or more operations for the symptoms under consideration.

No Previous Formal Psychiatric Care.—The proportion of improved patients was less among the 44 who had had previous psychiatric care than among the group as a whole.

Steady Employment.—There were 412 patients who were old enough to have been employed for several years and from whom adequate past employment histories could be obtained. The proportion of improved patients among the 280 who had been steadily employed was greater than that among the 132 who changed jobs frequently.

Duration of Present Illness Less Than Five Years.—There were 154 patients in whom symptoms referable to the present illness were of less than one year's duration on admission to the clinic; 75% of these were in the improved group. Of the 224 patients whose illness had lasted more than one year but less than five years, 69% were improved. In the 361 whose illness had lasted more than five years, only 63% were improved.

DATA DEPENDENT ON PATIENT'S INTERPRETATION

The following criteria distinguished those patients who showed the greatest improvement. The categories reflect the patient's own interpretation of his background and experience.

Previous Health Good (One Point).—Those who had had the usual childhood illnesses but no serious diseases or traumatic accidents were among those who showed most improvement.

Some Religious Education (One Point).—Among the improved, those patients who had had some religious education appeared in greater numbers. Fewer of those with a "strict" religious background (attendance at parochial schools) and family stress on religious observation or with no religious education and no family adherence to religious custom were found among the improved group.

Emotional Support from Both Parents (Four Points).—By emotional support from both parents was understood loving care of the child combined with predictable and consistent discipline in keeping with prevailing cultural patterns.

Congenial Siblings (Two Points). — This implied fondness among brothers and sisters, with competition for parental affection and recognition at a minimum.

Emotional Support from Spouse (Two Points).—Credit was given for evidence that the spouse customarily endorsed the patient in public and private and for evidence of mutual interdependence with a minimum of belittling criticism.

Sexual Compatibility with Spouse (Two Points).—Credit depended on an expression of satisfaction by the patient in his intimate sexual relations with his or her spouse.

No Serious Sexual Problem (Three Points).—Serious sexual problems were defined as deviations from the accepted form of sexual behavior in the form of homosexual relations or unusual sexual appetites when they were sources of anxiety and guilt.

Spouse Adequate Economic Provider (Two Points).—This item was included only for the female married patient on the basis of her evaluation of her husband's effectiveness as a provider.

Children Not Rejected (Two Points).—Evidence of rejection included both overt and implicit expression of hostility on the part of patients toward their children.

No Housing Problem (Two Points).—In evaluation of the patient's housing situation, the yardstick was not the standard of housing authorities or the physician, but the patient's own appraisal of his home surroundings. Living in a substandard tenement in a poor neighborhood, if not indicated by the patient as being a source of conflict or disturbance, was not considered a housing problem.

Occupational Satisfaction, Congenial Working Conditions, Moderately Adequate Salary (Two Points Each).—The exact nature of the work done, hours of work, salary obtained, and attitude toward fellow workers and superiors provided evidence of the patient's attitude toward his work. Satisfaction and pride in terms of individual needs were stressed. Scoring is intended to reflect the patient's attitudes toward various aspects of his working life. The score was not based on Department of Labor standards or on the physician's appraisal of the job and salary.

DATA DEPENDENT ON PHYSICIAN'S INTERPRETATION

Many individual attributes were appraised by the physician and found relevant to the patient's course in the clinic. These separate items have been classified into four main groups: (1) past performance, (2) personality structure, (3) attitude toward the present illness, and (4) potential modifiability of the current situation. Each group is weighted 10 points.

Past Performance.—In the evaluation of the patient's reaction to stress, the manner in which adversity had been met in the past was taken into account. The capacity for entering into and maintaining warm interpersonal relations and achieving a sexual adjustment was credited under the category of past performance. Also included was an estimate of the degree to which the patient had been able to derive satisfaction from the vocations and avocations of everyday life.

Personality Structure.—This was evaluated through an analysis of the balance of drives and characteristic behavior as revealed by a review of the life history as a whole and through a discussion of ordinary incidents in daily life. Evidence was sought to illustrate the patient's degree of flexibility and capacity to adapt to change. Indications of extreme hostility, overt or unexpressed, were considered of poor prognostic significance, especially if there were instances of asocial behavior.

A favorable interpretation was placed on indications of resourcefulness and stamina in dealing with personal problems as well as evidence of participation in civic, club, and church activities. Moderate but not excessive orderliness and reliability were also scored as good signs; finally, credit was given for indications of maturity of values and goals.

Attitude Toward the Present Illness.—The physician's evaluation of the patient was focused on an appraisal of the patient's attitude toward his illness. A "declaration of bankruptcy" in which the patient indicated a recognition of failure of past patterns of adjustment and his need for help in making new ones was considered the most favorable attitude. Another helpful indication was the willingness to consider the pertinence of stressful life

experiences as factors in bringing about illness. Confidence in the physician and the hospital and a capacity and willingness to assume some responsibility in treatment were other items in this group.

Modifiability.—Attempts were made to determine whether the onset of the patient's illness was contemporaneous with an environmental change, i. e., change of job, school, home environment, death or illness of a parent figure, or return from military service. If such were the case, the possibility of manipulating the environmental situation for the individual patient was evaluated.

METHOD OF APPLYING SCALE

The scoring of one patient is shown in table 1. He achieved 69%, and it was predicted that he would achieve symptomatic improvement without basic change. At the time of writing he had been seen in the clinic over a period of 27 months on 42 occasions—14 in the last 12 months as contrasted with 10 in the first 3 months. His course was a fluctuating one, varying not with the seasons but with the stressful situations at home. He had not missed more than three days at work during this period, compared with the weeks and months of absence in previous years.

TABLE 2.—*Comparison of Prognostic Scale Results with Appraisals of Patients' Clinical Status* *

Results	No. of Patients	Prognosis Rating	
		Range	Average
Migraine †			
Group 1	18 (35%)	41-61	52
Group 2	30 (58%)	60-74	65
Group 3	4 (7%)	79-83	81
Hypertension ‡			
Group 1	37 (41%)	25-62	51.8
Group 2	44 (49%)	51-58	63
Group 3	9 (10%)	80-89	82.5
Asthma §			
Group 1	18 (27%)	25-59	49.5
Group 2	33 (49%)	52-65	61
Group 3	16 (24%)	70-83	80

* Group 1, unimproved; group 2, symptomatically improved; and group 3, basically improved.
† Fifty-two patients. ‡ Ninety patients. § Sixty-seven patients.

TESTING OF THE PROGNOSTIC SCALE

The scale was applied to 67 patients with asthma, 52 with migraine, and 90 with essential hypertension treated by this medical group. Patients with these diagnoses were selected because they have a well-defined clinical syndrome in which changes in severity can be fairly reliably appraised. When the prognostic scale results were compared with the separately recorded appraisals of the patients' clinical status, a close correlation was observed (table 2).

The 73 patients with hypertension, asthma, or migraine headaches, who averaged a score below 60% on the prognosis score, were found in the unimproved group; only 5 who had been considered unimproved scored over 60%. The symptomatically or moderately improved group comprised 107 patients whose average score was 63%. Only one patient in this group scored above 73%, while five scored below 60%. In the third group of 29 basically improved patients the average score was 81%, with only one scoring below 71%.

Because in retrospect the criteria for improvement or lack of it appeared somewhat rough and not in sufficient detail, an attempt was made in the 90 cases of hypertension to appraise more carefully and in greater detail the clinical status at the time this report was prepared.

The 90 patients fell into four groups: Group 1, or "no change," included 37 patients, or 41% of the total. These patients showed no detectable change in blood pressure, in basic attitudes as defined earlier, or in other stress reactions.

Group 2, or "minor change," was made up of 38 patients, or 41% of the total. This group was further divided into three subgroups: subgroup A, with blood pressure the same, basic attitude only slightly changed or the same, and other stress reactions significantly reduced; subgroup B, with blood pressure lower, basic attitude the same, and other stress reactions reduced; and subgroup C, in which blood pressure became normal, other stress reactions were reduced, but the basic attitude remained the same.

Group 3, or "moderate change," included eight patients, or 9% of the total. In these the blood pressure was the same or slightly reduced, basic attitudes were moderately altered, and the other stress reactions were definitely reduced.

Group 4, or "major change," was made up of nine patients, or 10% of the total. In these the blood pressure had fallen to normal, the basic attitude was much altered, and other stress reactions were greatly reduced.

From an examination of these results, reported in detail in another publication,[2] it would appear that some alteration could be anticipated as a result of a constructive physician-patient relationship in approximately 60% of patients with essential hypertension who complain of symptoms. Most of these, or about 40% of the total, were those changed in that they had fewer symptoms, less outward expression of anxiety, and greater tranquillity than before the experience, although in most of these the blood pressure was not appreciably lowered. However, even in this group a slight lowering of the blood pressure was associated with a decline in symptoms and a restitution of some degree of tranquillity.

The symptom loss was not directly related to a change in the blood pressure level, although in group 4 the loss of symptoms was accompanied by a lowering of the blood pressure. Tremulousness, insomnia, and restlessness were most readily modified. Headache, mainly related to more or less superficially suppressed anger or frustration and to fatigue, was also modifiable and, as mentioned elsewhere,[3] was not related to the level of the blood pressure. These reactions were more easily modified than the blood pressure elevation, which was associated with more deeply repressed anger or frustration. Thus a consideration of life situations, attitudes, and feeling states reduced or eliminated symptoms and other stress reactions in the majority of those with essential hypertension and reduced the blood pressure to normotensive levels in a few. The prognostic scale was applied to the revised data obtained from the more detailed analysis of the clinical state of each patient with hypertension. The results corresponded even more closely than those listed in table 2.

2. Wolff, H. G., and Wolf, S.: Hypertension: A Symposium, Minneapolis, University of Minnesota Press, 1951, p. 457.
3. Wolff, H. G.: Headache and Other Head Pain, New York, Oxford University Press, 1948.

SUMMARY

The records of 739 patients with "stress" diseases treated by 18 physicians in the medical outpatient department of a university hospital have been studied and analyzed to determine which factors could be correlated with the degree of change observed in these patients in the course of treatment directed chiefly at the patient's personal adjustment to his life situation. Various factors that correlated with improvement were assembled into a scale for use as a clinical guide to prognosis in individual patients. This scale was applied to a group of 209 patients with asthma, migraine headaches, and hypertension, whose clinical course had already been evaluated. It was found that the patients scoring below 60% were in the unimproved group, those scoring between 65% and 75% were considered symptomatically improved, and those scoring over 80% were considered basically improved.

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EVALUATION OF NEW ADRENOLYTIC DRUG (REGITINE®) AS TEST FOR PHEOCHROMOCYTOMA

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The diagnosis of hypertension due to increased amounts of circulating epinephrine, arterenol, or both, released by pheochromocytoma is receiving more and more emphasis for two reasons. 1. It has only recently been recognized that many of these tumors cause sustained elevation of blood pressure, which is clinically indistinguishable from essential hypertension, and not paroxysmal attacks of hypertension. 2. Although pheochromocytomas are a comparatively uncommon cause of hypertension, if a correct diagnosis can be made and surgical removal of the tumor accomplished, the persistent elevation of the blood pressure can be decreased. The differential diagnosis, therefore, between essential hypertension, for which there is only palliative treatment, and that caused by a pheochromocytoma, for which there is surgical relief, is an important one.

Although clinical experience and diagnostic acumen may suggest strongly the presence of pheochromocytomas, the introduction of various pharmacologic agents as aids in diagnosis has greatly enhanced the accuracy of detecting their presence. These drugs have been divided into two groups: (1) those that induce the characteristic clinical symptoms and episodes of paroxysmal hypertension similar to the attacks that occur spontaneously, including histamine,[1] tetraethylammonium chloride or bromide,[2] and methacholine (mecholyl®) hydrochloride,[3] and (2) those that block the effects of the circulating pressor substance as shown by a substantial fall in the blood pressure of patients with persistent hypertension. Drugs in the latter group must have little or no depressor effect in hypertension of other origins. The drugs that have been most widely used on patients with persistently elevated blood pressure have been piperoxan [4] and dibenamine® [5] (N,N-dibenzyl-β-chloroethyl amine). Although piperoxan has frequently indicated accurately the presence of a pheochromocytoma, in our hands as in others it has not been infallible, for it gives false negative [6] as well as false positive results.[7] Dibenamine® will block the effect of circulating epinephrine and arterenol and will cause a drop in blood pressure when a pheochromocytoma is elaborating these substances.[5] Unfortunately, it likewise possesses depressor effects in the presence of essential hypertension,[8] and this greatly minimizes its value as a diagnostic agent.

Any test drug that will supplement piperoxan hydrochloride and dibenamine® will give one more aid in the diagnosis of this rare but important condition. Such a drug is regitine® (C-7337), first used and suggested by Grimson and co-workers.[9] Regitine® is the hydrochloride of 2-(N-*p*-tolyl-N-[*m*-hydroxyphenyl]-aminomethyl)-imidazoline and is related chemically to priscoline® (2-benzyl-2-imidazoline hydrochloride). Pharmacologically it possesses marked adrenolytic action in animals [10] and man.[11] Pressor effects resulting from infusions of both epinephrine and arterenol in dogs are blocked by regitine.® [12] For this reason regitine® has been used therapeutically in controlling the hypertensive crises of patients undergoing operations for removal of a pheochromocytoma.[9b,c] The present study is concerned with the effect of regitine® on normotensive persons, patients with hypertension, and patients with a pheochromocytoma.

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1. Roth, G. M., and Kvale, W. F.: A Tentative Test for Pheochromocytoma, Am. J. M. Sc. **210**: 653-660 (Nov.) 1945.

2. LaDue, J. S.; Murison, P. J., and Pack, G. T.: Use of Tetraethylammonium Bromide as a Diagnostic Test for Pheochromocytoma, Am. J. Med. **3**: 118 (July) 1947.

3. Evans, J. A.; Rubitsky, H. J.; Bartels, C. C., and Bartels, E. C.: Re-Evaluation of the Reliability of Pharmacologic and Cold Pressor Studies in Hypertension and Pheochromocytoma, Am. J. Med. **11**: 448-460 (Oct.) 1951. Guarneri, V., and Evans, J. A.: Pheochromocytoma: Report of a Case, with a New Diagnostic Test, ibid. **4**: 806-813 (June) 1948.

4. Goldenberg, M.; Snyder, C. H., and Aranow, H., Jr.: New Test for Hypertension Due to Circulating Epinephrine, J. A. M. A. **135**: 971-976 (Dec. 13) 1947.

5. Spear, H. C., and Griswold, D.: The Use of Dibenamine in Pheochromocytoma: Report of a Case, New England J. Med. **239**: 736-739 (Nov. 11) 1948.

6. Calkins, E.; Dana, G. W., and Howard, J. E.: Current Methods of Diagnosis of Pheochromocytoma, J. A. M. A. **145**: 880-883 (March 24) 1951. Mason, R. E.: Pheochromocytoma with False Negative Benzodioxane Tests, Am. J. Med. **11**: 524-530 (Oct.) 1951. Conley, J. E., and Junkerman, C. L.: Lack of Specificity of Piperoxan Hydrochloride Test for Adrenal Medullary Tumors, J. A. M. A. **147**: 921-923 (Nov. 3) 1951.

7. (*a*) Emlet, J. R.; Grimson, K. S.; Bell, D. M., and Orgain, E. S.: Use of Piperoxan and Regitine® as Routine Tests in Patients with Hypertension, J. A. M. A. **146**: 1383-1386 (Aug. 11) 1951. (*b*) Taliaferro, I.; Adams, R. A., and Haag, H. B.: Benzodioxan Test: Fall in Blood Pressure Following Its Use in a Case of Renal Hypertension, ibid. **140**: 1271-1273 (Aug. 20) 1949.